

REMARKS

Applicant's attorney wishes to thank the Examiner for the careful consideration given this case. Claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, and 27 are pending in this case. Herein, Claim 1 is amended. Newly-introduced Claim 31 introduces no new matter and is fully supported by the specification.

This response addresses those issues raised in the Office Action dated November 27, 2002. It is believed that the present amendments and following remarks render all pending claims allowable. Reconsideration of the claims as amended is respectfully requested.

The Examiner states that the present application is not in compliance with 37 C.F.R. 1.821 through 1.825. A substitute computer readable form of the sequence listings and the required statement accompany this response. It is respectfully submitted that the present application is presently in compliance with the appropriate rules.

The Examiner notes that one sheet of figures appears to be missing from the file. A duplicate copy was requested and is provided with this response.

The Examiner rejects Claims 1, 3, 5, 7, 9, 11, 13, 15, 17, and 27 under 35 U.S.C. § 102(b) as being anticipated by Brush *et al.* (U.S. Patent No. 5,986,086). It is submitted that the present amendments overcome this rejection. An important feature of the present invention resides in that the fluorescent nucleotide has no sulfonic acid group and no phosphoric acid group, while still maintaining a water soluble group at C. Examples of the water soluble group (sulfonamide, polyether, lower alcohol, and the like) are described on lines 11-13 of page 10 of the present

specification. Please also refer to Compounds 1 – 4 on page 21, which were used in the Examples of the application. Compounds 1 and 3 have a sulfonamide group, while Compounds 2 and 4 have an ether alcohol group. Brush *et al.* disclose a non-sulfonated cyanine dyes for labeling nucleotides, but do not teach a dye having a water soluble group such as a sulfonamide group. The advantage of the use of a dye having a water soluble group such as a sulfonamide group is described on the second paragraph of page 10 of the specification of the present application. It states:

However, especially fluorescent dyes of high molecular weights sometimes become to be insoluble due to reduction of functional groups having these negative charges. In one aspect of the present invention, the problem for these insolubility is solved by introducing a water-soluble functional group into a chromophore of a dye. For example, in one embodiment of the present invention, the fluorescent nucleotide is characterized in that it has a water-soluble group other than a sulfonic acid group in its fluorescent dye component. Water-soluble functional groups which can be introduced into the fluorescent dye include sulfonamide, polyether, lower alcohol, sugar chain, tertiary amine, quaternary ammonium salt and the like.

The advantages of the present invention are demonstrated in the Examples of the present application. The fluorescent intensities of Compounds 5-8 are stronger than the comparative dye Cy-5-dUTP (Amersham) or Cy-3-dUTP (Amersham) as shown in Tables 1 and 2 on pages 27 and 28 of the present application. The advantage of the present invention is achieved by using a dye having no sulfonic acid group and no phosphoric acid and having a water soluble group at C. None of the cited references teach the use of a dye having no sulfonic acid group and no phosphoric acid, while having a water soluble group. Reconsideration and withdrawal of the 102(b) rejection is respectfully requested.

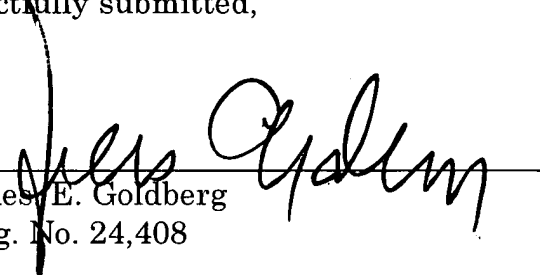
The Examiner rejects Claim 19 under 35 U.S.C. § 103(a) as being unpatentable over Brush *et al.* in view of Mao *et al.* As noted above, Claim 1 has

been amended to include the limitation that the fluorescent nucleotides of the present invention have no sulfonic acid group and no phosphoric acid group, while still maintaining a water soluble group at C. In light of this amendment, it is respectfully submitted that the cited references do not contain all of the claim limitations as set forth in the present claims. To establish a *prima facie* case of obviousness of a claimed invention, all of the claim limitations must be taught or suggested by the prior art. MPEP § 2143.03. In addition, all dependent claims depend properly from Claim 1 and are, therefore, submitted to be in condition for allowance. Accordingly, reconsideration and withdrawal of this obviousness rejection is respectfully requested.

In view of the amendments to the claims and the remarks presented herein, it is respectfully submitted that the present application is in condition for final allowance and notice to such effect is requested. If the Examiner believes that additional issues need to be resolved before this application can be passed to issue, the undersigned invites the Examiner to contact him at the telephone number provided below.

Respectfully submitted,

Dated: May 27, 2003

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